

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule encoding sGNK or a variant thereof.
2. An isolated nucleic acid molecule of claim 1, comprising a sequence selected from the group consisting of (a) the sequence of nucleotides in SEQ ID NO: 1, from nucleotide 1 to nucleotide 4610; (b) nucleic acid molecules capable of hybridization to a nucleic acid molecule of (a) under conditions of moderate stringency, and which encode sGNK; and (c) nucleic acid molecules which are degenerate, as a result of the genetic code, with respect to the nucleic acid molecules of (a) or (b).
3. An isolated nucleic acid molecule of claim 1, comprising a sequence selected from the group consisting of (a) the sequence of nucleotides in SEQ ID NO: 1, from nucleotide 75 to nucleotide 2549; (b) nucleic acid molecules capable of hybridization to a nucleic acid molecule of (a) under conditions of moderate stringency, and which encode sGNK; and (c) nucleic acid molecules which are degenerate, as a result of the genetic code, with respect to the nucleic acid molecules of (a) or (b).
4. A recombinant expression vector comprising a promoter operably linked to a nucleic acid molecule according to claim 1, 2, or 3.
5. A host cell containing the recombinant expression vector of claim 4.
6. An isolated sGNK polypeptide.
7. An isolated sGNK polypeptide that is encoded by the nucleic acid of one of claims 1-3.
8. An isolated sGNK polypeptide comprising an amino acid sequence that is at least 80% identical to SEQ ID NO: 2.
9. The sGNK polypeptide of claim 8 comprising the sequence SEQ ID NO: 2.
10. An isolated GNK comprising a sufficient number of amino acids from SEQ ID NO: 4 to confer on the polypeptide vascularization regulatory activity on cells of mammalian origin.
11. An isolated nucleic acid molecule comprising a sufficient number of nucleotides from SEQ ID NO: 3 to encode a polypeptide that regulates vascularization.

12. A recombinant expression vector comprising a promoter operably linked to the nucleic acid sequence of claim 11.
13. A host cell containing the recombinant expression vector of claim 12.
14. A method for producing a polypeptide having vascularization regulating activity comprising culturing the recombinant host cell according to claim 13 under suitable conditions to express the polypeptide encoded by the nucleic acid molecule.
15. The method of claim 14 wherein the host cell is a bacterial, yeast, insect or mammalian cell.
16. The method of claim 14 wherein the host cell is a COS cell.
17. The method of claim 14 wherein the host cell is a 293 cell.
18. A method for stimulating blood vessel development comprising administering a therapeutically effective amount of GNK or GNK agonist to a patient.
19. The method of claim 18 wherein the stimulation of blood vessel development promotes wound healing.
20. The method of claim 18 wherein the stimulation of blood vessel development reduces cardiac dysfunction.
21. A method of reducing blood vessel development comprising administering a therapeutically effective amount of a GNK antagonist to a patient.
22. The method of claim 21 wherein the reduction of blood vessel development slows or prevents tumor development.
23. A method for treating a vascularization disorder comprising the step of administering to a patient a therapeutically effective amount of a GNK antagonist.
24. The method of claim 23 wherein the vascularization disorder is psoriasis.
25. The method of claim 23 wherein the vascularization disorder is arthritis.
26. The method of claim 23 wherein the vascularization disorder is proliferative retinopathy.
27. A pharmaceutical composition comprising GNK.
28. A pharmaceutical composition comprising at least one GNK agonist.
29. A pharmaceutical composition comprising at least one GNK antagonist.

30. An antibody molecule, or fragment thereof, which binds specifically to the vascularization regulatory domain of GNK.

31. An antibody molecule, or fragment thereof, which binds specifically to a portion of the sGNK of one of claims 6-9.

32. The antibody molecule, or fragment thereof, of claim 31 which is a polyclonal antibody.

33. The antibody molecule, or fragment thereof, of claim 31 which is a monoclonal antibody.

34. A method for substantially purifying sGNK comprising:
coupling the antibody molecule, or fragment thereof, of any of claims 30 to 33, to a solid support to form a matrix that selectively binds sGNK;
applying a mixture of polypeptides containing the sGNK to the matrix;
introducing conditions under which the sGNK and the antibody molecule, or fragment thereof, form an antigen-antibody complex;
washing unbound components of the mixture of polypeptides from the matrix;
and
eluting the sGNK from the matrix.

35. A homologous recombination vector comprising a nucleotide sequence substantially similar to SEQ ID NO: 3, the sequence differing from SEQ ID NO: 3 by the addition, deletion, or substitution of one or more nucleotides to prevent expression of a polypeptide with vascularization regulatory capability, structurally linked to one or more selectable marker genes.

36. The homologous recombination vector of claim 35 wherein at least one selectable marker gene confers resistance to G418.

37. The homologous recombination vector of claim 35 wherein at least one selectable marker gene confers sensitivity to ganciclovir.

38. A method for generating GNK-deficient cells comprising:
transfecting cells with a homologous recombination vector that is incapable of expressing biologically active GNK and that contains a selectable marker;
selecting for transfected cells using selective medium;
propagating the transfected cells in culture; and
monitoring the propagated cells for GNK expression.

39. A method for identifying genes or gene products involved in regulating vascularization comprising:

propagating GNK-deficient cells or organs in parallel with wild-type cells or organs;

preparing parallel samples from the GNK-deficient and wild-type cells for analysis;

comparing the parallel GNK-deficient and wild-type samples for differential gene expression or protein modification; and

identifying the differentially expressed gene or differentially modified protein.

40. A method for identifying genes or gene products involved in regulating vascularization comprising:

propagating sGNK-deficient cells or organs in parallel with wild-type cells or organs;

preparing parallel samples from the sGNK-deficient and wild-type cells for analysis;

comparing the parallel sGNK-deficient and wild-type samples for differential gene expression or protein modification; and

identifying the differentially expressed gene or differentially modified protein.

41. A method of identifying a compound that modulates a protein-protein interaction between GNK and sGNK, comprising:

a) contacting a candidate compound with GNK and sGNK under conditions permitting the interaction between GNK and sGNK, and

b) measuring the ability of the candidate compound to modulate the interaction between GNK and sGNK.

42. A method of identifying a compound that modulates phosphorylation of sGNK by GNK, comprising:

a) contacting a candidate compound with GNK and sGNK under conditions permitting the phosphorylation of sGNK by GNK, and

b) measuring the ability of the candidate compound to modulate the phosphorylation of sGNK by GNK.

43. A method of identifying a compound that modulates vascularization comprising:

a) contacting a candidate compound with GNK or sGNK, and

b) measuring the ability of the candidate compound to modulate a biological activity of the GNK or sGNK.

44. A compound identifiable by a method according to one of claims 41-43.

45. The compound of claim 44 wherein the compound is selected from the group consisting of activators of GNK, inhibitors of GNK, activators of sGNK, inhibitors of sGNK, activators of an interaction between GNK and sGNK, inhibitors of the interaction between GNK and sGNK, activators of phosphorylation of sGNK by GNK, and inhibitors of phosphorylation of sGNK by GNK.

46. A nonhuman transgenic embryo, fetus, or animal that is heterozygous for a GNK targeted mutation.

47. A nonhuman GNK-deficient embryo or fetus produced by crossing heterozygous animals according to claim 46.

48. A cell from the embryo, fetus, or animal of claim 46 or 47.

49. A GNK deficient cell.

50. An sGNK deficient cell.

51. A recombinant vector comprising a promoter operably linked to a nucleic acid molecule encoding sGNK according to claim 8.

52. A host cell containing the recombinant expression vector of claim 51.

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